



**UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office**

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|-----------------|-------------|----------------------|---------------------|
|-----------------|-------------|----------------------|---------------------|

09/270,006 03/16/99 ROBIN

J 017753-113

021839 HM22/0312
BURNS DOANE SWECKER & MATHIS L L P
POST OFFICE BOX 1404
ALEXANDRIA VA 22313-1404

EXAMINER

BALASUBRAMANIAN.V

ART UNIT

PAPER NUMBER

1624

DATE MAILED:

03/12/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/270,006

Applicant(s)
Robin et al.

Examiner
Venkataraman Balasubramanian

Group Art Unit
1624



☒ Responsive to communication(s) filed on Dec 26, 2000

☒ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 88-101 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 88-101 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Art Unit: 1624

DETAILED ACTION

Applicants, response which included cancellation of claims 1-87 and addition of new claims 88-101 filed on 12/26/2000 is made of record.

Claims 88-101 are now pending.

In view of applicants' response ie cancellation of claims 1-87, all 112 rejections made in the previous office action have been rendered moot. Similarly, the newly presented claim 88-101, which are now limited to oxacycloalkane carboxylic acid and with provisos to exclude prior art compounds, have rendered all 102 rejections moot.

However, the following 103 rejection made in the previous office action remains.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 88-101(previously claims 59-65) are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. Yaoxue Xuebao (Acta. Pharm. Sinica)27, 178-184, 1992(Wang I) and Huang et al, the Alkaloids, Vol. XXII 157-225, 1984 in view of Wang et al. Yaoxue Xuebao (Acta. Pharm. Sinica)27, 173-177, 1992(Wang II) for reasons of record. To repeat:

Art Unit: 1624

Wang I teaches the tetrahydrofuran and tetrahydropyran esters of cephalotaxine as noted in the above 102 rejection. See compound 8 and 9. Note these compounds are known to exhibit antitumor activity.

Wang I differs in not making the tetrahydrofuran or pyran carboxylic acid first.

Huang et al. teaches the process for hydrolyzing the cephalotaxine alkaloids and the synthesis of the acid components. See page 165 for mild hydrolysis to get compound 7 and see route 3 on page 166. Wang II teaches a process for cyclizing the open chain acid ie compound 7 bearing a CTX group to the corresponding tetrahydrofuran compound. See page 174 of Wang II and note the last reaction shown at the bottom of the page using TsOH.

Note the starting materials are analogous in that they are compound of formula 7 with a methoxy on the tertiary carboxylic group or CTX. Thus one having ordinary skill in the art at the time of the invention was made would have been motivated to combine both the primary and secondary references and employ the process taught by these prior art to the starting materials and expect to obtain the desired product because he would have expected the analogous starting materials and reactants react similarly. It has been held that application of an old process to an analogous material to obtain a result consistent with the teachings of the art would have been obvious to one having ordinary skill. Note *In re Kerkhoven* 205 USPQ 1069.

Applicants argument to overcome this rejection is not persuasive.

Applicants argue that instant invention differs in using the chiral acid for making the final product which leads to even with racemate to diastereoisomers or enantiomerically pure product - a benefit not

Art Unit: 1624

suggested or taught by the cited reference. This is not a valid argument. It is well known in the art that chiral intermediates can be resolved and used for making enantiomerically pure compound or diastereoisomers as the case may be. Hence, one trained in the art would have been motivated to resolve the racemic acid taught by the prior art and use it for synthesis of chiral compounds.

Hence the rejection is proper and is maintained.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

As for references cited in the IDS, as noted in the previous office action, references which were properly cited in the Information Disclosure Statement have been considered but those missing , page numbers, book information etc. were not considered. Applicants should provide the missing information for consideration of those references.

Art Unit: 1624

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (703) 305-1674. The examiner can normally be reached on weekdays from 8.30 AM to 5.00 PM.

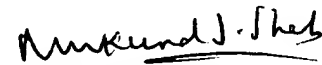
The fax phone number for the organization where this application or proceeding is assigned (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

V/B

V. Balasubramanian (Bala)

3/5/2001



MUKUND J. SHAH

SUPERVISORY PATENT EXAMINER

AU 1624